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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,922	08/29/2005	Gerard Papierok	1811-60	6168

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EXAMINER	
GANGLE, BRIAN J	
ART UNIT	PAPER NUMBER
1645	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,922	PAPIEROK ET AL.	
	Examiner	Art Unit	
	BRIAN J. GANGLE	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-21* is/are pending in the application.

4a) Of the above claim(s) *18-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/12/2007 has been entered.

The amendment and remarks, filed 12/12/2007, are acknowledged. Claims 1-15 are cancelled. New claims 16-21 are pending. Claims 18-21 are withdrawn as being drawn to non-elected inventions. Claims 16-17 are currently under examination.

Election/Restrictions

Newly submitted claims 18-21 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the originally examined claims are drawn to a product, whereas claims 12-15 are drawn to methods of using said product. As shown by the rejections under 35 USC 102, set forth in the previous office action, there is no special technical feature linking the product and the method claims.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 18-21 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Objections Withdrawn

The objection to the disclosure, because Trypan is improperly listed as a trademark, is withdrawn in light of applicant's amendment thereto.

Claim Rejections Withdrawn

The rejection of claim 10 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the phrase "the classes IgG2 and corresponding sub-classes." There is

no definition in the specification of the term "corresponding sub-classes," is withdrawn in light of the cancellation of said claim.

The rejection of claim 10 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the phrase "the major excreted-secreted immunogen," is withdrawn in light of the cancellation of said claim.

The rejection of claim 10 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the phrase "specific to the carboxyterminal part," is withdrawn in light of the cancellation of said claim.

The rejection of claim 10 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the phrase "said immunoglobulins being specific to a major immunogen, belonging to Protein Surface Antigens and corresponding to a range of molecular mass from 52 to 58 kDa," is withdrawn in light of the cancellation of said claim.

The rejection of claim 10 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the phrase "said immunoglobulins being specific to isotypes IgG2 in dogs and specific isotypes in other mammals," is withdrawn in light of the cancellation of said claim.

The rejection of claim 10 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite because the claim is drawn to a composition of immunoglobulins capable of lysing amastigotes and promastigotes of *Leishmania*, is withdrawn in light of the cancellation of said claim.

The rejection of claim 11 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the phrase "said immunoglobulins being markers for immunotherapy in leishmaniases and infections by pathogenic intracellular micro-organisms in mammals," is withdrawn in light of the cancellation of said claim.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, essentially for the reasons set forth in the rejection of claims 10-11 in the previous office action.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant argues:

1. That the overall aim of the invention disclosed in the present patent application is to offer a test allowing the distinction between infected dogs and immunized dogs.

2. That infected dogs generate antibodies, including IgG2, to antigens from *Leishmania* species, but they do not generate any IgG2 specific to the carboxyterminal part of the PSA protein. Applicant asserts that the PSA protein is a major antigen of the antigens excreted-secreted by *Leishmania* amastigotes and promastigotes. Applicant also asserts that only dogs immunized with the vaccine complex disclosed in French patent 01/07606 (US application 10/480,026) are able to generate IgG2 that are specific to the carboxyterminal part of the PSA protein.

3. That the present inventors contend that "when thy filed for patent protection initially in France in 2002, they began the research and development on the carboxyterminal part of the PSA protein."

4. That cryptic or immunologically silent epitopes are known to those of skill in the art. Applicant asserts that cryptic epitopes are silent until they are "unmasked." In the present invention, the epitope located in the carboxyterminal part of the PSA is silent in natural infection, but is "unmasked" in the context of an immunization by the vaccine complex disclosed

in related US application 10/480,026. Applicant contends that the epitopes in the carboxyterminal portion of the PSA is hidden except when the PSA is injected into dogs in the presence of an adjuvant, Because the presentation of the antigen to the immune system by the parasite may be different from that of soluble antibodies injected in the presence of an adjuvant.

5. That Figures 1-3 of the priority document disclose the carboxyterminal part of the PSA. Figure 1 shoes the protein surface antigens by name: A3B, 1A1, W2, and 2G1. Applicant asserts that Figure 2 shows the lack of IgG2 response against the C-terminal of the PSA in patients suffering from leishmaniasis and that Figure 3 shows the response from vaccinated dogs, which do produce an IgG2 response.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, while some of what is disclosed in the instant specification has to do with a test allowing distinction between infected dogs and immunized dogs, the issue at hand is what the claims are drawn to. The claims are not drawn to a test for recognizing immunized dogs, they are drawn to a composition for lysing amastigotes and promastigotes.

Regarding argument 2, applicant's assertions in this latest response are not consistent with the instant specification or the claims. In fact, the specification itself is internally inconsistent. The specification provides evidence that antibodies to the carboxyterminal part of PSA do exist in infected animals. In paragraph [0023] of the specification, applicant states, "after chemotherapy or immunotherapy, the IgG2s in dogs specific to the ES antigens of Leishmania and notably of the carboxyterminal part of PSA appear with significant improvement in the general state of dogs that have contracted *Leishmaniasis*." In paragraph [0079], applicant shows that 4 infected dogs that recovered from *Leishmania infantum* infection had IgG2 specific for the carboxyterminal part of the PSA. In paragraph [0082], the specification states links the capacity to produce these antibodies with recovery of infected animals. Moreover, the claims themselves indicate that the antibodies are markers for infections by pathogenic intracellular microorganisms (of which *Leishmania* is one). Therefore, while stating that infected dogs do not develop the antibodies, the specification provides evidence that infected dogs do actually generate the antibodies. This inconsistency provides further evidence that the description of the claimed invention is lacking.

In addition, while applicant asserts, in their arguments, that only dogs immunized with the vaccine complex disclosed in application 10/480,026 generate the claimed antibodies, the specification does not indicate this. The instant specification indicates (in addition to the above statements, which are at odds with this) that it is immunization with secretion-excretion antigens that leads to generation of the claimed antibodies (see paragraph [0017]). According to the instant specification and to application 10/480,026, these antigens are merely antigens that are naturally "excreted-secreted" by *Leishmania* amastigotes and promastigotes.

Regarding argument 3, it appears that applicant is admitting that they did not have possession of the claimed invention at the time of filing, since the research was begun when the application was filed. At the very least, it appears that priority to the French patent application should be reconsidered.

Regarding argument 4, those of skill in the art are aware of "cryptic" epitopes. As described by applicant, these are epitopes that are not normally exposed to the immune system and which would not generate antibodies until the block by another structure or some alteration of the three dimensional epitope occurs. However, there are multiple things that confuse this issue, illustrating the deficiencies of the written description. According to the instant specification and to application 10/480,026, the "vaccine" that leads to generation of the antibodies contains antigens that are naturally "excreted-secreted" by *Leishmania* amastigotes and promastigotes. If this were the case, applicants have shown no "unmasking" of the epitope and a natural infection would be expected to generate the claimed antibodies since the antigens are naturally secreted by the organisms. Alternatively, applicant states that the antigens are Protein Surface Antigens (PSAs), which the art shows are membrane bound proteins, which, by definition, are not excreted or secreted. If this is the case, it seems likely that, if the epitope where in the intracellular portion of the antigen, it would be hidden during infection and exposed upon vaccination with said antigen. However, administration of lysed cells would expose the immune system to this epitope and one would expect the claimed antibodies to develop upon such an administration. In addition, the claims are now drawn to antibodies that specific for this cryptic epitope that is not described in the instant application.

Regarding argument 5, there are no figures in the instant application and applicant has deleted any reference to figures in the application. Therefore, figures that might have been

present in a French priority document do not provide written description support for the claimed invention.

As outlined previously, the instant claims are drawn to a composition for inducing pathways leading to lysis of amastigotes and promastigotes of *Leishmania* sp. *in vitro*, said composition comprising immunoglobulins of IgG2 which are specific to the excretion-secretion antigens of promastigotes or amastigotes of *Leishmania* sp., and which are specific to an epitope located in a carboxyterminal part of Protein Surface Antigens A313, 1A1, W2 and 2G1 or in sequence 133A; wherein the immunoglobulins are markers of immunotherapy in leishmaniases and infections by pathogenic intracellular micro-organisms in mammals.

The rejected claims are drawn to a genus of antibodies, the members of which bind to the "excretion-secretion antigens" of promastigotes or amastigotes of *Leishmania* sp. and which must bind to some epitope located in a carboxyterminal part of Protein Surface Antigens A313, 1A1, W2 and 2G1 or in sequence 133A.

The courts have recently decided in Randolph J. Noelle v Seth Lederman, Leonard Chess and Michael J. Yellin (CAFC, 02-1187, 1/20/2004) that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See Enzo Biochem II, 323 F.3d at 965; Regents, 119 F.3d at 1568. Therefore, based on our past precedent, as long as an applicant has disclosed a "fully characterized antigen," either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen. Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application. Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the

ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application.

In the instant application, Applicant has failed to "fully characterize" both the antigen (i.e. excretion-secretion antigens) and the epitope to which the claimed antibody binds. Consequently, since Applicant has not fully characterized the antigen to which the claimed antibodies bind, the written description requirements under 35 U.S.C 112, first paragraph have not been met. To characterize an antigen, the immunoepitopes that can be found on said antigen must be identified. This characterization must not only include identification of epitopes that allow antigen-antibody binding, but also those that result in lysis of the microorganism.

The specification does not describe the excretion-secretion antigens to which the members of the claimed genus of antibodies must bind, such that the specification might reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed. Further, the antigen to which the antibodies must bind is a Protein Surface Antigen, which, according to the art, is a membrane protein, and therefore cannot be excreted or secreted (see Kemp *et al.*, FEMS Immunol. Med. Microbiol., 20:209-218, 1998, IDS filed 4/29/2005). The specification also lacks any mention of Protein Surface Antigens A313, 1A1, W2 and 2G1 or in sequence 133A and consequently does not disclose any specific epitopes on these antigens. Moreover, the names “A313, 1A1, W2, 2G1, and sequence 133A” are merely laboratory designations that do not provide any structural or functional information.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, ‘does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed’ ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed.

See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

As evidenced by Greenspan et al. (Nature Biotechnology 17: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might

profoundly affect binding. Accordingly, it follows the epitope to which any given antibody binds can only be identified empirically. Even using a competition assay, the skilled artisan cannot determine whether an antibody binds the same epitope as another antibody because an antibody that competes with another does not necessarily bind the same epitope as the other; rather, one antibody may bind a spatially overlapping epitope to sterically hinder binding of the other. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of epitopes to which the members of the claimed genus of antibodies must bind, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of antibodies. Moreover, since the specification has not identified which amino acids of the genus of epitopes to which the members of the claimed genus of antibodies must bind, which are critical or essential to the binding, one skilled in the art would not recognize that Applicant had possession of the claimed invention at the time the application was filed.

Therefore, in accordance with the *Guidelines*, the description of immunoglobulins is not deemed representative of the genus of immunoglobulins to which the claims refer.

Claims 16-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, essentially for the reasons set forth in the rejection of claims 10-11 in the previous office action

The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant argues:

1. That the overall aim of the invention disclosed in the present patent application is to offer a test allowing the distinction between infected dogs and immunized dogs.

2. That infected dogs generate antibodies, including IgG2, to antigens from *Leishmania* species, but they do not generate any IgG2 specific to the carboxyterminal part of the PSA protein. Applicant asserts that the PSA protein is a major antigen of the antigens excreted-secreted by *Leishmania* amastigotes and promastigotes. Applicant also asserts that only dogs immunized with the vaccine complex disclosed in French patent 01/07606 (US application

10/480,026) are able to generate IgG2 that are specific to the carboxyterminal part of the PSA protein.

3. That the present inventors contend that "when thy filed for patent protection initially in France in 2002, they began the research and development on the carboxyterminal part of the PSA protein."

4. That cryptic or immunologically silent epitopes are known to those of skill in the art. Applicant asserts that cryptic epitopes are silent until they are "unmasked." In the present invention, the epitope located in the carboxyterminal part of the PSA is silent in natural infection, but is "unmasked" in the context of an immunization by the vaccine complex disclosed in related US application 10/480,026. Applicant contends that the epitopes in the carboxyterminal portion of the PSA is hidden except when the PSA is injected into dogs in the presence of an adjuvant, Because the presentation of the antigen to the immune system by the parasite may be different from that of soluble antibodies injected in the presence of an adjuvant.

5. That Figures 1-3 of the priority document disclose the carboxyterminal part of the PSA. Figure 1 shoes the protein surface antigens by name: A3B, 1A1, W2, and 2G1. Applicant asserts that Figure 2 shows the lack of IgG2 response against the C-terminal of the PSA in patients suffering from leishmaniasis and that Figure 3 shows the response from vaccinated dogs, which do produce an IgG2 response.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, while some of what is disclosed in the instant specification has to do with a test allowing distinction between infected dogs and immunized dogs, the issue at hand is what the claims are drawn to. The claims are not drawn to a test for recognizing immunized dogs, they are drawn to a composition for lysing amastigotes and promastigotes.

Regarding argument 2, applicant's assertions in this latest response are not consistent with the instant specification or the claims. In fact, the specification itself is internally inconsistent. The specification provides evidence that antibodies to the carboxyterminal part of PSA do exist in infected animals. In paragraph [0023] of the specification, applicant states, "after chemotherapy or immunotherapy, the IgG2s in dogs specific to the ES antigens of Leishmania and notably of the carboxyterminal part of PSA appear with significant improvement in the general state of dogs that have contracted *Leishmaniasis*." In paragraph [0079], applicant shows

that 4 infected dogs that recovered from *Leishmania infantum* infection had IgG2 specific for the carboxyterminal part of the PSA. In paragraph [0082], the specification states links the capacity to produce these antibodies with recovery of infected animals. Moreover, the claims themselves indicate that the antibodies are markers for infections by pathogenic intracellular microorganisms (of which *Leishmania* is one). Therefore, while stating that infected dogs do not develop the antibodies, the specification provides evidence that infected dogs do actually generate the antibodies. This inconsistency provides further evidence of the unpredictability of the subject matter.

In addition, while applicant asserts, in their arguments, that only dogs immunized with the vaccine complex disclosed in application 10/480,026 generate the claimed antibodies, the specification does not indicate this. The instant specification indicates (in addition to the above statements, which are at odds with this) that it is immunization with secretion-excretion antigens that leads to generation of the claimed antibodies (see paragraph [0017]). According to the instant specification and to application 10/480,026, these antigens are merely antigens that are naturally "excreted-secreted" by *Leishmania* amastigotes and promastigotes.

Regarding argument 3, it appears that applicant is admitting that the claimed invention was not enabled at the time of filing, since the research was begun when the application was filed. At the very least, it appears that priority to the French patent application should be reconsidered.

Regarding argument 4, those of skill in the art are aware of "cryptic" epitopes. As described by applicant, these are epitopes that are not normally exposed to the immune system and which would not generate antibodies until the block by another structure or some alteration of the three dimensional epitope occurs. However, there are multiple things that confuse this issue, illustrating the deficiencies of the written description. According to the instant specification and to application 10/480,026, the "vaccine" that leads to generation of the antibodies contains antigens that are naturally "excreted-secreted" by *Leishmania* amastigotes and promastigotes. If this were the case, applicants have shown no "unmasking" of the epitope and a natural infection would be expected to generate the claimed antibodies since the antigens are naturally secreted by the organisms. Alternatively, applicant states that the antigens are Protein Surface Antigens (PSAs), which the art shows are membrane bound proteins, which, by

definition, are not excreted or secreted. If this is the case, it seems likely that, if the epitope where in the intracellular portion of the antigen, it would be hidden during infection and exposed upon vaccination with said antigen. However, administration of lysed cells would expose the immune system to this epitope and one would expect the claimed antibodies to develop upon such an administration. In addition, the claims are now drawn to antibodies that specific for this cryptic epitope that is not described in the instant application.

Regarding argument 5, there are no figures in the instant application and applicant has deleted any reference to figures in the application. Therefore, figures that might have been present in a French priority document do not provide support for the claimed invention.

As outlined previously, enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: The instant claims are drawn to a composition for inducing pathways leading to lysis of amastigotes and promastigotes of *Leishmania* sp. *in vitro*, said composition comprising immunoglobulins of IgG2 which are specific to the excretion-secretion antigens of promastigotes or amastigotes of *Leishmania* sp., and which are specific to an epitope

located in a carboxyterminal part of Protein Surface Antigens A313, 1A1, W2 and 2G1 or in sequence 133A; wherein the immunoglobulins are markers of immunotherapy in leishmaniases and infections by pathogenic intracellular micro-organisms in mammals.

Breadth of the claims: The claims encompass the genus of immunoglobulins of the class IgG2, the members of which bind to the "excretion-secretion antigens" of promastigotes or amastigotes of *Leishmania* sp. and which are specific to an epitope located in a carboxyterminal part of Protein Surface Antigens A313, 1A1, W2 and 2G1 or in sequence 133A.

Working Examples/Guidance of Specification: The specification fails to describe either the antigens or the immunoepitopes against which the claimed antibodies are raised and must subsequently bind. Nor do they disclose which immunoepitopes would result in the lysis, and consequent neutralization of the promastigotes or amastigotes of *Leishmania* sp. "Excretion-secretion antigens" are not defined, and the "major immunogen" which belongs to the family of Protein Surface Antigens is described only in that it has a mass from 52 to 58 kDa. However, Protein Surface Antigens are membrane bound proteins, which, by definition, are not excreted or secreted. Further, there is no disclosure of antibodies that are specific to Protein Surface Antigens with a mass from 52 to 58 kDa, nor is there disclosure of any antibodies capable of lysing amastigotes or promastigotes of *Leishmania* sp., let alone antibodies specific to Protein Surface Antigens with a mass from 52 to 58 kDa that are capable of binding or lysing amastigotes or promastigotes of *Leishmania* sp.

State of the Prior Art and Unpredictability of the Art: In the instant application, Applicant has failed to "fully characterize" the antigen (i.e. excretion-secretion antigens) to which the claimed antibody binds. Consequently, since Applicant has not fully characterized the antigen to which the claimed antibodies bind, the skilled artisan would not be able to make the claimed invention.

While the skill in the art of immunology is high, to date, prediction of a specific immune response for any given composition in any given animal is quite unpredictable. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie *et al.* (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of

these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie *et al.* further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie *et al.* further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Additionally, Greenspan *et al.* (Nature Biotechnology 17: 936-937, 1999), disclose defining epitopes is not as easy as it seems. Greenspan *et al.* recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan *et al.*, an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a protective immune response to a given pathogen can only be identified empirically. This constitutes undue experimentation.

In addition, applicant has not shown, and those of skill in the art would not expect, that any of the claimed antibodies would have anything to do with infections by any intracellular microorganism other than *Leishmania* species.

Therefore, given the lack of success in the art, the lack of working examples commensurate in scope to the claimed invention and the unpredictability of the generation of a directed immune response, the specification, as filed, is not enabling.

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Deplazes *et al.* (Parasite Immunol., 17:451-458, 1995, IDS filed 4/29/2005), essentially for the reasons set forth in the rejection of claims 10-11 in the previous office action.

Applicant argues:

1. That the claims of the present application are limited to dogs.

2. That the present invention is a composition of IgG2 antibodies specific to the carboxyterminal portion of an antigen in dogs immunized with antigens of the promastigote forms and amastigote forms of *Leishmania infantum*. Applicant asserts that these antibodies are only found in immunized dogs, and not in infected dogs. Applicant argues that the reference relates only to the IgG proteins of naturally leishmanian animals.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, contrary to applicant's assertion, the claims are not limited to dogs. The claims are drawn to immunoglobulins and there is no limitation that they be from dogs.

Regarding argument 2, applicant's assertions in this latest response are not consistent with the instant specification or the claims. In fact, the specification itself is internally inconsistent. The specification provides evidence that antibodies to the carboxyterminal part of PSA do exist in infected animals. In paragraph [0023] of the specification, applicant states, "after chemotherapy or immunotherapy, the IgG2s in dogs specific to the ES antigens of Leishmania and notably of the carboxyterminal part of PSA appear with significant improvement in the general state of dogs that have contracted *Leishmaniasis*." In paragraph [0079], applicant shows that 4 infected dogs that recovered from *Leishmania infantum* infection had IgG2 specific for the carboxyterminal part of the PSA. In paragraph [0082], the specification states links the capacity

to produce these antibodies with recovery of infected animals. Moreover, the claims themselves indicate that the antibodies are markers for infections by pathogenic intracellular microorganisms (of which *Leishmania* is one). Therefore, while stating that infected dogs do not develop the antibodies, the specification provides evidence that infected dogs do actually generate the antibodies.

Applicant has also asserted that the epitope to which the claimed antibodies bind is a "cryptic" epitope. As described by applicant, these are epitopes that are not normally exposed to the immune system and which would not generate antibodies until the block by another structure or some alteration of the three dimensional epitope occurs. However, acording to the instant specification and to application 10/480,026, the "vaccine" that leads to generation of the antibodies contains antigens that are naturally "excreted-secreted" by *Leishmania* amastigotes and promastigotes. If this were the case, applicants have shown no "unmasking" of the epitope and a natural infection would be expected to generate the claimed antibodies since the antigens are naturally secreted by the organisms. The Deplazes reference provides evidence of this in that they disclose an ELISA in which supernatant antigens from *Leishmania infantum* were used as the antigens to detect IgG2 (see page 452, final paragraph). Based on the specification and applicant's arguments, these are the same antigens that contain the appropriate epitope. Since applicant has provided no description (or claim limitations) of this epitope (other than to say it is in the carboxyterminal portion of the antigen), in the absence of evidence to the contrary, the IgG2 disclosed by Deplazes would necessarily contain the claimed antibodies.

As outlined previously, the instant claims are drawn to a composition for inducing pathways leading to lysis of amastigotes and promastigotes of *Leishmania* sp. *in vitro*, through activation of a complement cascade and inducing pathways leading to neutralization of proliferation of said amastigotes and promastigotes of *Leishmania* sp. in dogs, said composition comprising immunoglobulins of IgG2 which are specific to an epitope located in a carboxyterminal part of Protein Surface Antigens A313, 1A1, W2 and 2G1 or in sequence 133A; wherein the immunoglobulins are markers of immunotherapy in leishmaniases and infections by pathogenic intracellular micro-organisms in mammals.

Deplazes *et al.* disclose IgG2 antibodies obtained from dogs that are infected with *Leishmania infantum* (see page 454, column 2, paragraph 2). Because the "excretion-secretion"

antigens produced by promastigotes and amastigotes of *Leishmania* sp. are naturally produced by these organisms, a dog that is infected by *Leishmania infantum* would necessarily produce antibodies specific to the excretion-secretion antigens produced by promastigotes and amastigotes of *Leishmania* sp., including the major immunogen corresponding to a range of molecular mass from 52 to 58 kDa, and including antibodies specific to the carboxyterminal part of the major immunogen. Further, these antibodies would necessarily include antibodies having the same functional characteristics as the claimed antibodies. Finally, since the Patent Office does not have the facilities for examining and comparing Applicant's composition with the compositions of the prior art reference, the burden is upon Applicant to show a distinction between the material, structural and functional characteristics of the claimed composition and the composition of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 16-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Afrin *et al.* (Infect. Immun., 65:2371-2377, 1997), essentially for the reasons set forth in the rejection of claims 10-11 in the previous office action.

Applicant argues:

1. That the claims of the present application are limited to dogs.

2. That the present invention is a composition of IgG2 antibodies specific to the carboxyterminal portion of an antigen in dogs immunized with antigens of the promastigote forms and amastigote forms of *Leishmania infantum*. Applicant asserts that these antibodies are only found in immunized dogs, and not in infected dogs. Applicant argues that the reference discloses IgG2 from mice immunized with antigens of *L. donovani* rather than IgG2 that are selectively generated in dogs immunized with excretion-secretion antigens. Therefore, the invention describes antibodies against the carboxyterminal part of an antigen not described in the Afrin reference.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, contrary to applicant's assertion, the claims are not limited to dogs. The claims are drawn to immunoglobulins and there is no limitation that they be from dogs.

Regarding argument 2, applicant's assertions in this latest response are not consistent with the instant specification or the claims. In fact, the specification itself is internally inconsistent. The specification provides evidence that antibodies to the carboxyterminal part of PSA do exist in infected animals. In paragraph [0023] of the specification, applicant states, "after chemotherapy or immunotherapy, the IgG2s in dogs specific to the ES antigens of Leishmania and notably of the carboxyterminal part of PSA appear with significant improvement in the general state of dogs that have contracted *Leishmaniasis*." In paragraph [0079], applicant shows that 4 infected dogs that recovered from *Leishmania infantum* infection had IgG2 specific for the carboxyterminal part of the PSA. In paragraph [0082], the specification states links the capacity to produce these antibodies with recovery of infected animals. Moreover, the claims themselves indicate that the antibodies are markers for infections by pathogenic intracellular microorganisms (of which *Leishmania* is one). Therefore, while stating that infected dogs do not develop the antibodies, the specification provides evidence that infected dogs do actually generate the antibodies.

Applicant has also asserted that the epitope to which the claimed antibodies bind is a "cryptic" epitope. As described by applicant, these are epitopes that are not normally exposed to the immune system and which would not generate antibodies until the block by another structure or some alteration of the three dimensional epitope occurs. However, acording to the instant specification and to application 10/480,026, the "vaccine" that leads to generation of the antibodies contains antigens that are naturally "excreted-secreted" by *Leishmania* amastigotes and promastigotes. If this were the case, applicants have shown no "unmasking" of the epitope and a natural infection would be expected to generate the claimed antibodies since the antigens are naturally secreted by the organisms. Furthermore, as stated by applicant, the animals in Afrin were immunized using antigens from *Leishmania* (see page 2372, column 1, paragraphs 4-6). These antigens were obtained from lysed *Leishmania* promastigotes and culture supernatant and would necessarily contain the antigens used by applicant. These antigens would be in the same form as described by applicant and would thus have any "cryptic" epitopes exposed. Therefore, the IgG2 of these immunized animals would necessarily contain the claimed IgG2 antibodies. Applicant has shown no reason that the immune response generated by hamsters and mice would

be any different that the immune response of dogs and those of skill in the art would expect the antibody response of these animals to be similar.

As outlined previously, the instant claims are drawn to a composition for inducing pathways leading to lysis of amastigotes and promastigotes of *Leishmania* sp. *in vitro*, through activation of a complement cascade and inducing pathways leading to neutralization of proliferation of said amastigotes and promastigotes of *Leishmania* sp. in dogs, said composition comprising immunoglobulins of IgG2 which are specific to an epitope located in a carboxyterminal part of Protein Surface Antigens A313, 1A1, W2 and 2G1 or in sequence 133A; wherein the immunoglobulins are markers of immunotherapy in leishmaniases and infections by pathogenic intracellular micro-organisms in mammals.

Afrin *et al.* disclose IgG2 antibodies obtained from mice that have been immunized with *Leishmania donovani* promastigote antigens, as well as from mice that are infected with *Leishmania donovani* (see page 2372, column 1, paragraph 4). Because the Protein Surface Antigens produced by promastigotes and amastigotes of *Leishmania* sp. are naturally produced by these organisms, a mouse that is immunized with *Leishmania donovani* would have produced antibodies specific to the excretion-secretion antigens produced by promastigotes and amastigotes of *Leishmania* sp., including the major immunogen corresponding to a range of molecular mass from 52 to 58 kDa, and including antibodies specific to the carboxyterminal part of the major immunogen. Further, these antibodies would necessarily include antibodies having the same functional characteristics as the claimed antibodies. Finally, since the Patent Office does not have the facilities for examining and comparing Applicant's composition with the compositions of the prior art reference, the burden is upon Applicant to show a distinction between the material, structural and functional characteristics of the claimed composition and the composition of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 16-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Sartori *et al.* (Clin. Exp. Immunol., 87:386-392, 1992), essentially for the reasons set forth in the rejection of claims 10-11 in the previous office action.

Applicant argues:

1. That the claims of the present application are limited to dogs.

2. That the present invention is a composition of IgG2 antibodies specific to the carboxyterminal portion of an antigen in dogs immunized with antigens of the promastigote forms and amastigote forms of *Leishmania infantum*. Applicant asserts that these antibodies are only found in immunized dogs, and not in infected dogs. Applicant argues that the reference relates only to the IgG proteins of naturally leishmanian animals.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, contrary to applicant's assertion, the claims are not limited to dogs. The claims are drawn to immunoglobulins and there is no limitation that they be from dogs.

Regarding argument 2, applicant's assertions in this latest response are not consistent with the instant specification or the claims. In fact, the specification itself is internally inconsistent. The specification provides evidence that antibodies to the carboxyterminal part of PSA do exist in infected animals. In paragraph [0023] of the specification, applicant states, "after chemotherapy or immunotherapy, the IgG2s in dogs specific to the ES antigens of Leishmania and notably of the carboxyterminal part of PSA appear with significant improvement in the general state of dogs that have contracted *Leishmaniasis*." In paragraph [0079], applicant shows that 4 infected dogs that recovered from *Leishmania infantum* infection had IgG2 specific for the carboxyterminal part of the PSA. In paragraph [0082], the specification states links the capacity to produce these antibodies with recovery of infected animals. Moreover, the claims themselves indicate that the antibodies are markers for infections by pathogenic intracellular microorganisms (of which *Leishmania* is one). Therefore, while stating that infected dogs do not develop the antibodies, the specification provides evidence that infected dogs do actually generate the antibodies.

Applicant has also asserted that the epitope to which the claimed antibodies bind is a "cryptic" epitope. As described by applicant, these are epitopes that are not normally exposed to the immune system and which would not generate antibodies until the block by another structure or some alteration of the three dimensional epitope occurs. However, acording to the instant specification and to application 10/480,026, the "vaccine" that leads to generation of the antibodies contains antigens that are naturally "excreted-secreted" by *Leishmania* amastigotes and promastigotes. If this were the case, applicants have shown no "unmasking" of the epitope

and a natural infection would be expected to generate the claimed antibodies since the antigens are naturally secreted by the organisms. The Sartori reference provides evidence of this in that a 52 kD antigen was detected in renal eluates from the infected animals using a Western blot and immunoprecipitation (see abstract). Based on the specification and applicant's arguments, this is the same antigen that contains the appropriate epitope. Since applicant has provided no description (or claim limitations) of this epitope (other than to say it is in the carboxyterminal portion of the antigen), in the absence of evidence to the contrary, the IgG2 disclosed by Sartori would necessarily contain the claimed antibodies.

As outlined previously, the instant claims are drawn to a composition for inducing pathways leading to lysis of amastigotes and promastigotes of *Leishmania* sp. *in vitro*, through activation of a complement cascade and inducing pathways leading to neutralization of proliferation of said amastigotes and promastigotes of *Leishmania* sp. in dogs, said composition comprising immunoglobulins of IgG2 which are specific to an epitope located in a carboxyterminal part of Protein Surface Antigens A313, 1A1, W2 and 2G1 or in sequence 133A; wherein the immunoglobulins are markers of immunotherapy in leishmaniases and infections by pathogenic intracellular micro-organisms in mammals.

Sartori *et al.* disclose IgG2 antibodies obtained from hamsters that have been infected with *Leishmania donovani* promastigote antigens (see page 389, column 1, paragraph 2). Because the Protein Surface Antigens produced by promastigotes and amastigotes of *Leishmania* sp. are naturally produced by these organisms, a hamster that is infected by *Leishmania donovani* would have produced antibodies specific to the excretion-secretion antigens produced by promastigotes and amastigotes of *Leishmania* sp., including the major immunogen corresponding to a range of molecular mass from 52 to 58 kDa, and including antibodies specific to the carboxyterminal part of the major immunogen. Sartori *et al.* show that the antigens to which the hamsters have been exposed include a 52 kD antigen from *Leishmania donovani.* Further, these antibodies would necessarily include antibodies having the same functional characteristics as the claimed antibodies. Finally, since the Patent Office does not have the facilities for examining and comparing Applicant's composition with the compositions of the prior art reference, the burden is upon Applicant to show a distinction between the material, structural and functional

characteristics of the claimed composition and the composition of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

New Claim Rejections

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has amended claim 16 to recite "said epitope being located in a carboxyterminal part of Protein Surface Antigens A313, 1A1, W2 and 2G1 or in sequence 133A." Protein Surface Antigens A313, 1A1, W2 and 2G1 or in sequence 133A do not appear in the specification or original claims as filed. While mention is made of these antigens in the figures of the foreign priority document, these figures were not included in either the PCT or US filing of the instant application, and reference to the figures (said reference to the figures did not include any mention of Protein Surface Antigens A313, 1A1, W2 and 2G1) was deleted by applicant in response to an objection raised in the office action of 9/27/2006. Therefore, this limitation is new matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-17 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 is rendered vague and indefinite by the phrase "composition for inducing pathways leading to lysis of amastigotes and promastigotes of *Leishmania sp.* in vitro, through activation of a complement cascade and inducing pathways leading to neutralization of proliferation of said amastigotes and promastigotes of *Leishmania sp.* in dogs immunized with a vaccine complex." It is not clear what the intended use of the composition is. It is not clear if there are meant to be two intended uses (i.e. inducing lysis *in vitro* and inducing neutralization in immunized dogs) or one intended use (i.e. inducing lysis *in vitro*) and this use happens through activating the complement cascade and through inducing neutralization. If it is the latter, how can an *in vitro* use induce pathways in immunized dogs? If it is the former, applicant has argued, in support of this limitation, that the general principles of cell-mediated immune response are known to those of skill in the art. However, it is not clear what cell-mediated immune responses would develop *in vitro* and which pathways would be available *in vitro*. Furthermore, if an intended use is to neutralize proliferation of *Leishmania*, this appears to be a form of passive immunization, but it is not clear how a dog being immunized with a vaccine complex (that is not necessarily a *Leishmania* vaccine) prior to the passive immunization would have anything to do with said passive immunization. In addition, it is not clear what a "vaccine complex" is or how it differs from a vaccine. This rejection affects all dependent claims.

Claim 16 is rendered vague and indefinite by the phrase "said epitope being located in a carboxyterminal part of Protein Surface Antigens A313, 1A1, W2 and 2G1 or in sequence 133A." First, there is no definition provided in the specification for the term "carboxyterminal part." Therefore, it is not clear what limitations are engendered by this term. What are the limits of the "carboxyterminal part"? Applicant has previously argued that the "carboxyterminal part" is sufficiently described in the specification to mean the last part of the protein immunogen molecule, after repeated patterns rich in leucine, as defined in prior art. The examiner has found no such description in the specification or the art, and applicant has not pointed out where this information can be found. Applicant has not provided a sequence for the putative immunogen, thus one would be unable to determine which region is "rich in leucine." Furthermore, the term "rich" is a relative term for which the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In addition, the terms "A313," "1A1," "W2," "2G1," and "sequence

133A" are laboratory designations that do not provide any structural or functional limitations. This rejection affects all dependent claims.

Claim 17 is rendered vague and indefinite by the phrase "said immunoglobulins being markers for immunotherapy in leishmaniases and infections by pathogenic intracellular micro-organisms in mammals." It is not clear what is meant by the phrase "markers for immunotherapy." Does this mean that one can determine whether a given animal has received immunotherapy, or that one should provide immunotherapy for a given animal? How would one determine whether a mammal had received immunotherapy for cancer by searching for antibodies to *Leishmania* sp.?

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRIAN J. GANGLE whose telephone number is (571)272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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